I. Remarks

Claims 1-16 are currently pending.

Claims 1-3 and 10-12 are under consideration on the merits.

Claims 4-9 and 13-16 stand withdrawn pursuant to a restriction requirement. Applicant would like to pursue the withdrawn process claims eligible for rejoinder said embodiments when allowable subject matter is found with respect to the product claims currently under prosecution.

Applicant also notes that the Office has discusses a SEQ ID NO: 25 at page 10 of the Office Action mailed on September 26, 2005. Applicant believes that this was an inadvertent error and that it is not material to the rejection as set forth. Therefore, while the rejections as they pertain to SEQ ID NO: 25 and MART-1 have not been addressed in this response, Applicant believes in good faith that the instant response is fully responsive. Should Applicant's good faith belief be incorrect, Applicant respectfully requests clarification.

II. Claim rejections under 35 U.S.C. § 112

Claims 1-3 and 10-12 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. The Office has concluded that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the Office has concluded that the instant invention cannot be practiced without undue experimentation to determine whether each of the individual ligands, SEQ ID NOs: 3, 5, 7, or 9, recited in the instant claims are able to stimulate an effective immune response against the native ligand of SEQ ID NO. 11 and/ or the native eIF3-p40 protein. Applicant respectfully traverses.

The factors to be considered in determining enablement include the breadth of the claims, the nature of the invention, the state of the prior art, the skill level of the artisan, the predictability in the art, the direction provided by Applicant, the existence of working examples, and the quantity of experimentation required to make and/or use the invention based on the specification. A review of these factors demonstrates that the instant specification provides enabling support. The experimentation required to utilize the individual ligands, SEQ ID NOs: 3, 5, 7, or 9, or to determine their ability to stimulate an effective immune response against the native ligand is not undue. The instant specification provides the artisan with considerable guidance and direction, one of ordinary skill in the art could routinely perform any requisite experimentation at the time the application was filed, and the methods needed to practice the invention were well-known in the art.

1. The breadth of the claims and the nature of the invention

The instant invention is broadly drawn to various peptide compositions that comprise peptides from a selected group of sequences. The nature of the instant invention is directed to compositions comprising peptides selected from a specifically defined group of five sequences. The group of peptide sequences consists of SEQ ID NOs: 3, 5, 7, 9, or 11.

2. The guidance and direction provided by the specification and the level of ordinary skill in the art

The instant specification contains considerable guidance and direction with respect to the practice of the instant invention. It teaches that the compounds of the instant invention (SEQ ID NOs: 3, 5, 7, and 9) are synthetic antigenic peptide sequences, which are variations based on the native peptide epitope of eIF3 located at amino acids 242-250 of the eIF3 protein[1]. The instant specification expressly teaches that SEQ ID NO: 11 represents the "natural epitope of human cancer antigen eIF3"[2]. Applicant notes that the instant specification expressly states that all four of the instantly claimed ligands, SEQ ID NOs: 3, 5, 7, and 9, are cross-reactive and useful for modulating immune responses to their cognate native ligand (e.g. SEQ ID NO. 11) and their corresponding native protein (e.g. eIF3-p40)[3]. It teaches that the peptides are useful as components of anti-cancer vaccines and to expand immune effector cells that are specific for cells and cancer cells characterized by expression of the human cancer antigen eIF3[4]. As such, the specification discloses several manners and processes of making and using the instant invention which correspond to those used in describing the subject matter. Therefore, the guidance in the specification must enable an artisan to make and use the instantly claimed compositions in one of the disclosed processes. Applicant asserts that such enabling guidance is provided.

First, peptide synthesis was routine at the time of filing. This is evident in both the specification as well as in the state of the prior art. The specification provides guidance to synthesize the peptides of the instant invention[5]. A review of the prior art cited by the Office also demonstrates the routine practice of peptide synthesis. See, for example, Anderson et al. at page 520; Feltkamp et al. at page 1392; Guichard et al. at page 3804; and Valmori et al. at page 1751.

Second, the immunogenicity of the compounds and compositions of the instant invention was determinable using routine methods known at the time of filing. The specification provides no less than

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[1] See instant specification at page 5, lines 24-25 and page 25, line 25 - page 26, line 2. Applicants further note that amino acids 242-250 represent the amino acid sequence of SEQ ID. NO: 11.
[2] See instant specification at page 6, line 2. Therefore, in contrast to the Office's conclusion at page 5 of the Office Action mailed September 26, 2005, the specification identifies SEQ ID NO: 11 as a fragment of the eIF3 protein.
[3] See instant specification at page 24, lines 1-3.
[4] See instant specification at page 25, line 25 - page 26, line 2
[5] See instant specification at page 41, lines 7-31.

10 specific means by which an artisan could determine such immunogenicity[6]. These range from chromium-release lysis assays (CTL assay) to the use of transgenic animal models to the monitoring of T-cell receptor signal transduction. Applicant notes that the instant specification associates each of these 10 assays with at least one cited prior art reference. This is indicative that artisans, at the time of filing, practiced and knew these methods. Indeed, the prior art cited by the Office also evidences that such assays were known and practiced in the art. See, for example, van der Burg et al. at page 3309; Sarma et al. at page 812, and Valmori et al. at page 1752.

Third, the instant specification provides detailed guidance both in the instant specification, as well as by citation by reference, for using the claimed compositions to expand immune effector cells[7]. It also provides such guidance with respect to adoptive immune therapy and vaccines using such cells[8]

Therefore, the specification discloses more than one manner and process of making and using the instant invention which correspond to those used in describing the subject matter. Applicant notes that the standard is one of objective enablement- it matters not whether the enabling teachings are provided through broad terminology or through illustrative examples. In re Marzocchi, 439 F.2d 220, 223. Further, without a reason to doubt the truth the teachings provided by the instant specification, including the teachings that the instant compounds are cross-reactive with the native ligand, the disclosure must be taken as enabled.

3. The predictability in the art

The Office has concluded that there is considerably unpredictability in the art with respect to synthesizing functional equivalents of known epitopes. Applicant respectfully asserts that it is not relevant to the enablement of the instant invention whether there may be unpredictability in synthesizing functional equivalents of known epitopes. In the instant case, the claimed invention is drawn to compositions of specific compounds that the instant specification teaches are cross-reactive with the native epitope and protein. As such, the artisan is not searching for compounds reactive against eIF3 where unpredictability with respect to synthesizing functional equivalents might be relevant. There is no experimentation required to identify cross-reactive peptides. Rather, the artisan is presented with specific compounds of known sequence. Therefore, the experimentation required, if any, is to determine whether the peptides of the instant invention are cross-reactive with the eIF3 antigen. Applicant asserts that this comprises only routine experimentation at the time the application was filed.

4. The working example and the quantity of experimentation required to practice the invention as claimed

[6] See instant specification at page 46, line 27 - page 48, line 32.
[7] See instant specification at page 49, lines 1-20.

Moreover, the instant specification provides a specific demonstration that two of the instantly claimed ligands, SEQ ID NOs: 7 and 9, stimulate greater cytolytic activity against target cells than does the native ligand, SEQ ID NO. 11. This disclosure is provided in Figure 1, which a skilled artisan would recognize as the results from a CTL assay. It discloses "the cytolytic activity of two of the peptides of this invention as compared to the native epitope."[9] A review of Figure 1 reveals that the two peptides tested exhibit significantly greater specific lysis than the native epitope in its pure form. This graphically demonstrates that the instant peptide compounds are cross-reactive with the cognate native ligand.

While the instant specification does not experimentally demonstrate the cross-reactivity of SEQ ID NOs: 3 and 5, Applicant asserts that this is not fatal to the enablement quesiton. One of ordinary skill, assisted by the considerable guidance in the specification, could easily determine the immunogenicity of SEQ ID NOs: 3 and 5 against the native ligand of SEQ ID NO. 11 and/ or the native eIF3. As discussed *supra*, the immunogenicity of the compounds was determinable using routine methods known at the time of filing. This is evident in both the specification as well as in the state of the prior art. The specification itself sets forth 10 specific means by which an artisan could determine such immunogenicity[10]. For example, one of ordinary skill in the art could perform a chromium-release lysis assay, an assay routinely practiced in the art at the time of filing[11], to determine whether the peptide ligands, SEQ ID NOs: 3 and 5, are reactive against the native ligand of SEQ ID NO. 11 and/or the native eIF3. Applicant asserts that this represents only a reasonable quantity of routine experimentation to make and use the instant invention, if any is required.

Therefore, Applicant respectfully disagrees with the Office's conclusion that the instant invention cannot be practiced without undue experimentation to determine whether each of the individual ligands, SEQ ID NOs: 3, 5, 7, or 9, recited in the instant claims are able to stimulate an effective immune response against the native ligand of SEQ ID NO. 11 and/ or the native eIF3-p40 protein. A review of the required factors demonstrates that the instant specification provides enabling support. The experimentation required to utilize the individual ligands, SEQ ID NOs: 3, 5, 7, or 9, or to determine their ability to stimulate an effective immune response against the native ligand is not undue. There is the considerable guidance and direction provided by the specification, one of ordinary skill in the art could routinely perform any required experimentation, and the methods needed to practice the invention were well-known in the art. Accordingly, Applicant respectfully requests withdrawal of the instant rejection and allowance of the claims.

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[8] See instant specification at page 53, lines 1-24.
[9] See instant specification at page 5, lines 15-17 and Figure 1.
[10] See instant specification at ¶¶ [0197] - [0208].
[11] See, for example, van der Burg et al. at page 3309.

III. Conclusion

No fee is deemed necessary in connection with the filing of this communication. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 07-1074.

Respectfully submitted,

3/3/06
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